The Effects of Dopamine, Dobutamine and Amrinone on Mitochondrial Function in Cardiogenic Shock

Shuji Mukae, MD, Toshikuni Yanagishita, MD, Eiichi Geshi, MD, Kazuhiko Umetsu, MD, Masataka Tomita, MD, Seiji Itoh, MD, Noburu Konno, MD, and Takashi Katagiri, MD

SUMMARY

The impairment of mitochondria in non-infarcted myocardium under cardiogenic shock complicated by acute myocardial infarction was studied.

We induced acute myocardial infarction in dogs by ligating the circumflex branch of the left coronary artery (LCX). On basis of left ventricular systolic pressure (LVSP) after 60 minutes, we divided the dogs into two groups: a group in which LVSPs fell to below 70% of the pre-LCX ligation level, and a Control group in which LVSPs remained more than 90%. The former group was further divided into four subgroups, depending on infusion of dopamine, dobutamine, amrinone or saline after 90 minutes. Mitochondria were prepared and mitochondrial respiratory activity determined.

In the Saline group, hemodynamics became reduced to less than 70% of the preligation level after 120 minutes, however, in the Dopamine and Dobutamine groups, hemodynamics became restored to the preligation level. In the Amrinone group, LVSPs decreased slightly, while cardiac output, LV Max. dp/dt and myocardial blood flow increased. In the Saline group, mitochondria in the non-infarcted myocardium functioned at a lower level of activity than that of the Control group. However, in the Dopamine, Dobutamine, and Amrinone groups, the mitochondria functioned at a higher level. Electron microscopy revealed mitochondrial damage in the Saline group only.

The results indicate that an energy production disorder in the non-infarcted myocardium may have pathogenetic implications in cardiogenic shock associated with acute myocardial infarction, while dopamine, dobutamine, and amrinone improve mitochondrial function, and ultimately improve cardiac function. (Jpn Heart J 1997; 38: 515–529)

Key words: Acute myocardial infarction, Cardiogenic shock, Mitochondria, Dopamine, Dobutamine, Amrinone
RECENT advances in therapeutics in the coronary care unit (CCU) have greatly improved the prognosis for patients with acute myocardial infarction. However, the mortality rate remains high when severe pump failure such as cardiogenic shock occurs. Cardiotonic glycosides, catecholamines (dopamine and dobutamine), diuretics, phosphodiesterase inhibitors (amrinone and milrinone), vasodilators, and myocardial metabolism activators, all of which have different mechanisms of action and act on different sites in the myocardium and blood vessels, are used alone or in combination with other drugs to treat cardiogenic shock. Advances in molecular biology and biochemistry have clarified the mechanism of muscular contraction and relaxation. Furthermore, these advances will eventually serve to elucidate the mechanism of action of the aforementioned drugs in clinical use.1-5

In this study, we evaluated the effects of catecholamine (dopamine and dobutamine) and a phosphodiesterase inhibitor (amrinone) on cardiogenic shock complicated by acute myocardial infarction, for which the prognosis is still poor. To study the mechanism of action in cardiac metabolism, we utilized a dog experimental cardiac infarction model to study mitochondrial energy production. Mitochondria are the main cellular energy producing system and play a very important role in the energy metabolism of cardiac heart muscle.

Although the size of infarcted myocardium and cardiogenic reserve function have until now been considered to be mainly related to the cause of the cardiogenic shock,19-21 no specific causes of cardiogenic shock in the substructural level have yet been established. Hence, we focused our attention on the metabolism of non-infarcted myocardium, especially on mitochondrial function in acute myocardial infarction and studied energy production disorders at the substructural level. On the other hand, excessive catecholamine administration, which accelerates Ca influx into cells, has been raised as a cause of cellular injury6 and the effect of these drugs on the myocardial cell is a subject of interest. Therefore, this study primarily examines the effects of these agents on non-infarcted reserve function in acute myocardial infarction.

MATERIALS AND METHODS

Production of an experimental acute myocardial infarction model: Thirty mongrel dogs weighing 8 to 14 kg were anesthetized with intravenous ethylcarbamate (450 mg/kg), α-chloralose (45 mg/kg), and diazepam (10 mg), and then intubated for regulated respiration with room air. Following left thoracotomy at the fifth intercostal space, the circumflex branch of the left coronary artery (LCX) was separated. A pigtail catheter and a Swan-Ganz catheter were inserted into the femoral artery and vein to monitor left ventricular pressure, pulmonary
artery pressure, cardiac output (CO), and maximal linear differentiation of left ventricular systolic pressure (LV Max. dp/dt). A platinum electrode was inserted in the subendocardial layer at a site 2 mm from the endocardial layer, and regional myocardial blood flow in the center of perfusion in the anterior descending branch of the left coronary artery (LAD) and in the LCX was determined using the hydrogen gas clearance method. After these hemodynamic parameters were recorded at the preligation level, the LCX was ligated 1 cm from the origin to induce myocardial infarction. Acute myocardial infarction was identified by a persistent increase of 0.5 mV or more in the ST segment at II, III, and aVf on ECG, and by a decline in regional myocardial blood flow.

**Classification into shock and non-shock groups:** One criterion of cardiogenic shock in experimental acute myocardial infarction models is a decrease in left ventricular systolic pressure (LVPs) to less than 70% of the preligation level. Animals were assigned to groups according to the level of left ventricular systolic pressure 60 minutes after LCX ligation. One of these groups contained 19 dogs, all of whose LVPs fell to below 70% of the preligation level 60 minutes after LCX ligation; this group was deemed the Shock group \( (n=19) \). In the other group, LVPs was maintained at 90% or more of the preligation level 60 minutes after LCX ligation; this group was deemed the Control group \( (n=11) \). Intravenous drip infusion to dogs in the Shock group \( (n=19) \) was administered 90 minutes after ligation in the following manner. The dogs of the Shock group were divided further into four subgroups 90 minutes after LCX ligation: dopamine HCl \( (10 \mu g/kg/minute; \text{DOA group, } n=3) \); dobutamine HCl \( (10 \mu g/kg/minute; \text{DOB group, } n=3) \); amrinone \( (60 \mu g/kg/minute; \text{AMR group, } n=4) \); and 0.9% saline \( (10 \mu g/kg/minute; \text{Saline group, } n=9) \). The Shock group and Control group were observed for 120 minutes after ligation, the hearts extirpated, and the LAD and LCX regions removed as specimens.

**Extraction of mitochondria:** The beating heart of each dog was removed quickly 120 minutes after ligation, washed briefly in ice-cold saline solution, and placed on crushed ice. All procedures were undertaken at 4°C unless otherwise stated. Non-infarcted myocardium was collected from the LAD perfusion area and infarcted myocardium from the LCX area. Each myocardium was put on a petri dish on ice, and divided into two parts, the subendocardium and the subepicardium, and mitochondrial fraction was prepared. These pieces were sectioned, homogenized in 0.25M sucrose, 0.01M EGTA (glycoletherdiaminetetraacetic acid) and 0.03 M tris-HCl buffer (pH 7.4) using a Polytron. Homogenized samples were centrifuged at 27,000 × G. The sediment of each sample was treated with 1 mg alkaliprotease, further homogenized in 0.18 M KCl, 10 mM EGTA, 0.5% bovine serum albumin, and 0.03 M tris-HCl buffer (pH 7.4), and then centrifuged at 500 × G. The supernatant was further centri-
fuged twice at 12,000 × G and then used as a mitochondrial fraction which was treated with ultrasound to produce submitochondrial particles. The biuret method was used to determine the amount of protein in the mitochondria.

**Determination of mitochondrial respiratory activity:** Mitochondrial respiratory activity was determined by following the method with a polarograph (Yanagimoto PO-100A). Mitochondria and respiratory substrates (0.2 M succinic acid, or 0.2 M glutamic acid/malic acid) were placed in a buffer (pH 7.4) of 0.01 M KCl, 0.1 mM EDTA, 2 mM MgCl₂, 0.25 M sucrose, and 0.02 M potassium phosphate. 0.05 M ADP was then added. State 3 and State 4 respiratory activities were estimated as mitochondrial function at 25°C by decreases in the oxygen level.

**Determination of enzyme activities in the electron transport system of mitochondria:** Electron transport system enzyme activities were determined through the submitochondrial particles produced by ultrasonic treatment.

- **NADH-CoQ reductase (complex I) activity.** The method of Hatefi was used to spectrophotometrically measure changes in NADH levels at 340 nm.
- **Succinate dehydrogenase-CoQ reductase (complex II) activity.** The method of Ziegler was used to spectrophotometrically measure changes in 2,6-dichloroindophenol (DCIP) levels at 600 nm.
- **Cytochrome oxidase (complex IV) activity.** Conversion of the reduced form of cytochrome to its oxidized form was determined spectrophotometrically at 550 nm following the method of Orii.
- **Dinitrophenol (DNP)-dependent ATPase (complex V) activity.** The amount of phosphorus liberated from ATP in the presence of dinitrophenol was determined via Fiske-Subbarow’s method.

**Electron microscope:** A portion of each non-infarcted and infarcted myocardial tissue was removed immediately from the heart. The tissue was cut into small pieces and prefixed in a cold fixative solution of 2% glutaraldehyde in 0.1 M Na-cacodylate (pH 7.4) for 2 hours at 4°C. After being rinsed three times in 0.1 M Na-cacodylate (pH 7.4), these portions were postfixed in 2% osmium tetroxide (OsO₄) in 0.1 M cacodylate (pH 7.4) for 1 hour at 4°C, dehydrated in a graded series of ethanol and propylene oxide, and embedded in a mixture of Epon-Araldite. Ultrathin sections were cut from Epon-Araldite embedded tissues with a Sorball Porterblum ultramicrotome MT-2, double-stained with uranyl acetate and lead citrate, and examined with a Hitachi H-300 electron microscope.

**Statistical analysis:** Student’s t test was used to statistically analyze results at a significance of p < 0.05. All values are expressed as the mean ± SE.
RESULTS

Figure 1-A shows the chronological changes in LVPs. In the Control group, LVPs was maintained at more than 93.3% of the preligation level after 120 minutes. In the DOA, DOB, AMR, and Saline groups, dopamine (10 µg/kg/min), dobutamine (10 µg/kg/min), amrinone (60 µg/kg/min) and 0.9% saline (10 µg/kg/min) was administered, respectively, via intravenous drip infusion after 90 minutes of ligation. In the Saline group, LVPs decreased significantly after 120 minutes and became 58.6% of the preligation level. In the DOA and DOB groups, LVPs recovered noticeably after 120 minutes: the DOA group to 84.2%, and the DOB group to 94.3% of the preligation level. However, in the AMR group, LVPs decreased slightly after 120 minutes, and was 62.2% of the preligation level.

Figures 1-B and C show LV Max. dp/dt and cardiac output (CO). The tendency was the same for LVPs in the Control, Saline, DOA and DOB groups. In the AMR group, LV Max. dp/dt and cardiac output slightly recovered.

Figure 1-D shows regional myocardial blood flow (MBF) in the non-infarcted myocardium. The MBF in the Control group was preserved at over 98.0% of the preligation level 120 minutes after ligation. In the Saline group, however, the MBF decreased significantly, and after 120 minutes fell to 61.8% of the preligation level. In contrast, in the DOA and DOB groups, MBF recovered remarkably to 85.7% and 86.2% after 120 minutes, respectively. MBF recovery in the AMR group (66.9%) was moderate compared to the DOA and DOB groups.

The diagram is not presented but there are no significant hemodynamic differences (LVPs, LV Max. dp/dt, CO, MBF) between the groups (DOA, DOB, AMR, the Saline groups) from 0 minutes to 90 minutes after ligation.

We calculated the respiratory control index (RCI), which represents the ratio of state 3 to state 4 respiratory activity, to estimate mitochondrial energy production. Succinic acid or glutamic acid/malic acid were used as respiratory substrates. Figure 2 shows the RCI of mitochondria in the non-infarcted myocardium; succinic acid served as the respiratory substrate. In the Control group, the RCI were 4.81 ± 0.36 for the subendocardial muscle and 4.17 ± 0.23 for the subepicardial muscle; the values remained at normal levels. However, in the Saline group, the RCI of the subendocardial (p < 0.01) and subepicardial muscle (p < 0.001) at 3.25 ± 0.21 and 2.79 ± 0.18, respectively, underwent significant reduction.

In the DOA group treated with dopamine, values of 4.77 ± 0.19 for the subendocardial muscle (p < 0.01) and 4.57 ± 0.29 for the subepicardial muscle (p < 0.01) were significantly higher than those of the Saline group. In the DOB
Figure 1. Relative change in hemodynamics.

○ = Control group (n = 11, 0–120 minutes); ● = Shock group (n = 19, 0–90 minutes) or Saline group (n = 9, 90–120 minutes); △ = Dopamine (DOA) group (n = 3, 90–120 minutes), or Dobutamine (DOB) group (n = 3, 90–120 minutes), or Aminone (AMR) group (n = 4, 90–120 minutes).

LVPs = left ventricular systolic pressure; LV Max. dp/dt = maximal linear differentiation of left ventricular systolic pressure, CO = cardiac output; MBF = regional myocardial blood flow (in the non-infarcted myocardium).

Control group vs Shock group or Saline group: *p < 0.05, **p < 0.01, ***p < 0.001

DOA, or DOB, or AMR group vs Saline group: *p < 0.05, **p < 0.01, ***p < 0.001

In the Saline group, values of all parameters decreased markedly. However, these values in the Control group showed no significant change. In the DOA and DOB groups, these parameters recovered markedly. In the AMR group, LVPs decreased slightly, but LV Max. dp/dt, CO, and MBF in the non-infarcted myocardium recovered.
Figure 2. Mitochondrial respiratory control index (RCI) in the non-infarcted myocardium (succinic acid served as substrate). Control = Control group; Saline = Saline group; DOA = Dopamine group; DOB = Dobutamine group; AMR = Amrinone group. ■ subendocardial muscle; □ subepicardial muscle. Control group vs Saline group: **p < 0.01, ***p < 0.001. DOA, or DOB, or AMR group vs Saline group: **p < 0.01, ***p < 0.001. In the Saline group, significant reduction was observed in RCI, but in the DOA, DOB, and AMR groups, RCI increased markedly.

Figure 3. Mitochondrial respiratory control index (RCI) in the non-infarcted myocardium (glutamic acid/malic acid served as substrates). RCI was reduced in the Saline group, but RCI improved significantly in the DOA, DOB, and AMR groups.

group, the values of $4.47 \pm 0.03$ for the subendocardial muscle ($p < 0.01$) and $4.33 \pm 0.18$ for the subepicardial muscle ($p < 0.001$) were also significantly higher than those of the Saline group. In the Amrinone group, values of $5.10 \pm 0.40$ for the subendocardial muscle ($p < 0.001$) and $4.40 \pm 0.24$ for the subepicardial
muscle \((p < 0.001)\) were also significantly higher than those of the Saline group. As illustrated in Figure 3, when glutamic acid/malic acid were used as the respiratory substrates, similar changes were observed.

Consistent with the findings,\(^{15,16}\) the RCI in the infarcted myocardium of all groups were significantly lower than for the RCI in the non-infarcted myocardium. Figures 4-A, B, and C show the correlation between RCI in the non-infarcted myocardium and regional myocardial blood flow (MBF) in the non-infarcted myocardium. A significant correlation was observed between RCI and MBF: Figure 4-A presents the Control and Saline groups, and Figure 4-B the Control, Saline, DOA and DOB groups. However, as illustrated in Figure 4-C, the AMR group showed no significant correlation between RCI and MBF.

In addition, we measured the activity of enzymes in the mitochondrial electron transport system to determine what part of the system was injured,\(^{16}\) thereby causing the fall in mitochondrial respiratory control index. Figure 5 shows NADH-CoQ reductase (complex I) activity in the non-infarcted myocardium. In the Control group, the activity at 0.0650 ± 0.0048 (μ moles NADH per mg of protein per minute) for the subendocardial muscle and 0.0553 ± 0.0029 for the subepicardial muscle, was similar to the values for the normal myocardium.\(^{15,16}\) However, the values of the Saline group, which exhibited 0.0382 ± 0.0053 for the subendocardial muscle \((p < 0.01)\) and 0.0349 ± 0.0017
Figure 5. NADH-CoQ reductase (complex I) activity in the non-infarcted myocardial mitochondria. ■: subendocardial muscle; ▲: subepicardial muscle. Control group vs Saline group: ***p < 0.01; ****p < 0.001. DOA, or DOB, or AMR group vs Saline group: **p < 0.01. In the Saline group, complex I activity was remarkably lower than that in the Control group. Complex I activity was improved in the DOA, DOB, and AMR groups.

Figure 6. Dinitrophenol (DNP)-dependent ATPase (complex V) activity in the non-infarcted myocardial mitochondria. ■: subendocardial muscle; ▲: subepicardial muscle. Control group vs Saline group: *p < 0.05; **p < 0.01. In the Saline group, DNP-ATPase activity was reduced significantly. DNP-ATPase activity recovered in the DOA and DOB groups. On the contrary, in the AMR group, the activity showed no marked difference compared with that in the Saline group.

for the subepicardial muscle (p < 0.001) were considerably lower than those of the Control group. When catecholamines were administered, these values recovered; the DOA group was 0.0598 ± 0.0094 for subendocardial muscle and 0.0572 ± 0.0052 for subepicardial muscle (p < 0.01). The DOB group was 0.0572 ± 0.0052 for subendocardial and 0.0676 ± 0.0094 for subepicardial muscle (p < 0.01). The AMR group with 0.0683 ± 0.0052 for subendocardial
muscle \( p < 0.01 \) and 0.0585 ± 0.0052 for subepicardial muscle \( p < 0.01 \) exhibited a significant increase. On the contrary, in all groups, NADH-CoQ reductase activities in the infarcted myocardium were much lower than those in the non-infarcted myocardium. Furthermore, the decreased activity in the infarcted myocardium could not be normalized through the administration of catecholamine or phosphodiesterase inhibitor. Among the groups and between the non-infarcted myocardium and infarcted myocardium, there was no significant difference in succinate dehydrogenase-CoQ reductase (complex II) activity nor cytochrome oxidase (complex IV) activity (data not shown).

Figure 6 shows dinitrophenol (DNP)-dependent ATPase (complex V) activity in non-infarcted myocardium. Activity in the Control group was 12.91 ± 0.67 (µ moles Pi per mg of protein per hour) for subendocardial muscle and 10.54 ± 0.51 for subepicardial muscle, and remained at normal levels.\(^{15,16}\) In the Saline group, activity was 8.87 ± 0.85 for subendocardial \( p < 0.01 \) and 8.40 ± 0.70 for subepicardial muscle \( p < 0.05 \) showing a significant decrease. In the DOA group, the activity of subendocardial muscle was 11.96 ± 0.84 and subepicardial muscle 11.14 ± 0.34. In the DOB group, the values were 11.90 ± 0.43 and 10.62 ± 0.48, respectively. Both the DOA and DOB groups showed recovery. In the AMR group, the activity of subendocardial muscle was 7.91 ± 1.32 and subepicardial muscle 8.74 ± 1.60 exhibiting no noticeable difference compared to the Saline group. DNP-ATPase activity in the infarcted myocardium had considerably reduced activity for this enzyme, upon which the administration of catecholamine or amrinone had no effect.

Figure 7 shows electron micrographs of myocardial cells from each group.
Figure 7-A is non-infarcted myocardial cells in the DOA group. Myofibrils, mitochondria, and the T system remained normal, and no remarkable abnormal changes were observed in the ultrastructures; these results agree with a previous report. The fine structural changes in non-infarcted myocardial cells of the DOB and AMR groups were similar to those in the DOA group with normal ultrastructures (not shown). Figure 7-B is non-infarcted myocardial cells in the Saline group and reveals the swelling and fusion of mitochondria.

On the other hand, Figure 7-C shows infarcted myocardial cells in the Control group, which displayed necrotic cellular injury, including myofibrillar disruption, degradation of mitochondrial cristae, and dense deposits within mitochondria, as reported in a previous paper. The infarcted myocardial cells in other groups (DOA, DOB, AMR, and Saline groups) also exhibited necrotic cellular injury (not shown).

**Discussion**

The cause of cardiogenic shock complicated by acute myocardial infarction has been studied by focusing on the mitochondrial energy production system of non-infarcted myocardium.

The etiology of cardiogenic shock has long been considered mainly in relation to the size of the infarction. However, other factors such as differences in the coronary artery, distribution in compensated catecholamine secretions, and differences in compliance in the infarcted myocardium should also be taken into consideration because there are several papers which indicate that the size of the infarcted area is not the sole factor in the origin of cardiogenic shock. Wyatt demonstrated that functional depression in the non-ischemic myocardium is potentially important for understanding the mechanisms regulating cardiac performance. In terms of morphology, Vikhert found that mitochondrial damage, including swelling, opening of the matrix, and a decrease in the number of cristae in the non-occluded region of rabbit myocardium were important. Thus, no specific causes have yet been established. Therefore, we focus our attention on the metabolism of non-infarcted myocardium under cardiogenic shock in acute myocardial infarction, and study mitochondrial function in order to clarify the metabolism of cardiogenic shock at the substructural level.

Since we did not measure the size of the infarction, we are not sure whether there is a difference in the infarct size between the Shock and Control groups. However, we are certain that infarction large size is only one of the triggers that causes cardiogenic shock, and cardiogenic shock was induced by a combination of several factors. In our study, we studied the metabolic changes that followed hypoperfusion.
Previously, we have reported\textsuperscript{25,26} that one of the factors underlying cardiogenic shock is a malignant cycle in the non-infarcted myocardium. In short, when cardiogenic shock occurs, the reduction in perfusion in the non-infarcted myocardium decreases mitochondrial respiratory function in the energy production system, and injures the Ca\textsuperscript{2+}-ATPase of sarcoplasmic reticulum in the energy consumption system; this metabolic damage worsen cardiac function.

In the present study, we used catecholamines (dopamine, dobutamine) and a phosphodiesterase inhibitor (amrinone), both of which have been used clinically and found to be effective for the treatment of cardiogenic shock and left ventricular dysfunction. We also studied their effects on the aforementioned malignant cycle using mitochondrial respiratory activity and cardiac function as indices for myocardial metabolism.

Dopamine, an endogenous catecholamine, is a precursor of norepinephrine. It acts on $\beta$-receptors of the myocardium to increase contractility, and on the $\alpha$-receptors in the periphery to induce vasoconstriction.\textsuperscript{27} Dobutamine is a semi-synthetic catecholamine that acts on the $\beta_1$ receptors of the myocardium to increase contractility. Dobutamine is reported to improve coronary perfusion, decrease oxygen consumption, and induce a direct vasodilatory effect.\textsuperscript{28} Amrinone, a bipyridine inhibitor of type III phosphodiesterase, increases the cyclic AMP level in the myocardium. There are several studies\textsuperscript{27-31} regarding the mechanism of amrinone in cardiac metabolism. Amrinone has been documented as triggering improved cardiac performance without increasing myocardial oxygen consumption by reducing the left ventricular systolic wall stress that is caused by peripheral arteriolar vasodilatation.

Several reports\textsuperscript{3,32-34} on the hemodynamic and clinical effects of dopamine, dobutamine, and amrinone precede our study, but few have discussed the effects of catecholamines or phosphodiesterase inhibitors on myocardial failure at the substructural level.

Our study showed that in non-infarcted myocardium, the RCI of mitochondria in the Saline group decreased, and that the electron transport system (complex I and V activities) decreased in relation to the reduction of myocardial blood flow. We deduced that reduced regional myocardial blood flow injures the electron transport system of mitochondria, particularly complex I and complex V activities, and reduces mitochondrial respiratory activity. Furthermore, the energy production disorder diminishes myocardial contractility and accelerates the reduction of perfusion, leading to a malignant cycle of metabolisms. We believe that cardiogenic shock occurs through these mechanisms.

Also demonstrated was the fact that catecholamine (dopamine and dobutamine) administration elevates the left ventricular systolic pressure and regional myocardial blood flow in the non-infarcted myocardium, both of which
are associated with improved mitochondrial respiratory function. By means of positive inotropic action, catecholamine seems to activate mitochondrial respiratory function through hemodynamics. In contrast, while amrinone did not significantly increase LVPs, it slightly elevated MBF and CO and improved LV Max. dp/dt. Without markedly improving hemodynamics, amrinone restored mitochondrial respiratory activity to the Control group level. It is evident that both catecholamine and amrinone increase cyclic AMP levels and activate mitochondrial respiratory function. However, the mechanisms of increasing cyclic AMP and their effects on hemodynamics are different in catecholamine and amrinone. Hence, it is interesting to note the different mechanisms on myocardial cells when cardiogenic shock occurs. We think that sympathetic nerves and mitochondria are related; when we use catecholamine or amrinone, the difference in mitochondrial function and hemodynamics results from the difference in the effects of catecholamine or amrinone on sympathetic nerves. We also surmise that these drugs increase intracellular calcium, which stimulates NADH supply to the respiratory chain, and that the mechanisms of these effects by catecholamine or amrinone are different.

The above results suggest that both catecholamine and amrinone, though they operate under different mechanisms, activate mitochondrial respiratory function, and improve cardiac function by breaking the malignant cycle in the non-infarcted myocardium.

The current study reveals that in non-infarcted myocardium of acute myocardial infarction, the reduction of left ventricular systolic pressure decreases regional myocardial blood flow and results in the reduction of mitochondrial respiratory function. Furthermore, this dysfunction is improved by catecholamine and amrinone, both of which interfere with the pathogenic process of cardiogenic shock. Therefore, we believe that the improvement of metabolic disorders in the non-infarcted myocardium is crucial to the treatment of cardiogenic shock.

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